



Office of Pesticide Programs

FEB 15 2002

MEMORANDUM

SUBJECT: Non-dietary Exposure/Risk Assessment for Dolphin Antimicrobial (N-Butyl-1,2-Benzisothiazolin-3-one, new active ingredient) during manufacturing and residential consumer use of impregnated plastic products.

From: Siroos Mostaghimi, Ph.D., Environmental Engineer *Siroos - Mostaghimi*
Team One
Risk Assessment and Science Support Branch (RASSB)
Antimicrobials Division (7510C)

To: Marshall Swindell PM#33
Regulatory management Branch I
Antimicrobials Division (7510C)

Thru: Winston Dang, Team Leader *Winston Dang*
Team One
Risk Assessment and Science Support Branch (RASSB)
Antimicrobials Division (7510C)

Norm Cook, Chief *Norm Cook*
Risk Assessment and Science Support Branch (RASSB)
Antimicrobials Division (7510C)

DP Barcode: D270042, D272198, D272211, D272213, D272215, D272216, D272220

Pesticide Chemical No.: 098951

EPA MRID No.: 450830-01, 450830-02, 450830-03, 450830-04, 450830-05,

Review Time: 120 Hours

PHED: Yes

*Non-dietary Expt/
Risk Assessment*

NOTE:

The following risk assessment for Dolphin fungicide is based on the data provided by the registrant. The Risk Assessment and Science Support Branch has the following concerns about the use of these products:

- The toxicity endpoints used in this assessment are provided by the registrant. The Antimicrobials Division has not yet developed toxicity endpoints for this product because of the deficiency in the toxicity data base.
- The leaching data which were used to develop assessments may not be applicable to all types of plastics and all uses of this product.
- The labeling data does not indicate that the proposed treated plastics are for non-food uses only. There are several uses such as pond/ditch liners, garden hoses, conveyer belts, etc which may be considered as dietary use. Such uses would require RASSB dietary exposure and risk analysis.
- The present MOE analyses are based on the assumption that these products are not used in children's toys (as implied by the submitted risk assessments), but are used only in pet toys. The registrant needs to clarify this, for if these products are used in children toys, then further RASSB MOE analyses will be required.

Because of the above concerns AD reserves the right to revisit this risk assessment after the completion of the toxicity data base and development of the Toxicity endpoints by our toxicologists.

1.0 SUMMARY and CONCLUSIONS

Based on the estimated MOEs, the exposure scenarios in which MOEs for Dolphin antimicrobial are **larger than 100** and the short-term and immediate-term risks are identified as follows:

- Occupational handler short term and intermediate-term exposures during manufacturing of Dolphin-impregnated PVC products;
- Short term and intermediate-term residential exposures to Dolphin-impregnated shower curtains during showering for adults, females, and toddlers.
- Toddler short term and intermediate-term dermal and ingestion exposures during handling and mouthing Dolphin-impregnated pet toys.

- Residential short term exposures to Dolphin-impregnated polyurethane foam mattresses during sleeping for adults, females, and toddlers.
- Aggregated residential short term exposures to shower curtains during showering, mattresses during sleeping, and pet toys during handling and mouthing for adults, females, and toddlers.

The exposure scenarios in which the MOE is **less than 100** and of concern are identified as follows (Table 13):

- Residential intermediate term exposures to Dolphin-impregnated mattresses for adults, females, and toddlers (MOEs are 57, 48, and 27, respectively);
- Aggregated residential intermediate-term exposures to more than one Dolphin-impregnated plastic products (Aggregate MOEs are 56, 47, and 26, respectively).

2.0 INTRODUCTION

The purpose of this report is to assess occupational and residential non-dietary exposures to the Dolphin antimicrobial (i.e., N-Butyl-1,2- Benzisothiazolin-3-one), during manufacturing and residential consumer use of Dolphin-impregnated plastic products. The Dolphin (or Vanquish) antimicrobial is used to control the growth of fungi and bacteria in plastic products and therefore extend the life span of plastic products. Dolphin-treated plastic materials such as polyvinylchloride (PVS), silicone, and polyurethane are used to make a variety of products such as shower curtains, artificial leathers, and mattresses. The exposures to Dolphin antimicrobial were assessed for the following four worst-case exposure scenarios:

- Occupational exposures during production of a PVC master batch;
- Post-application residential exposure due to body contact with shower curtains during showering;
- Post-application residential exposure due to sleeping on the foam mattress; and
- Post-application residential exposure to toddlers due to playing with pet toys.

These exposure scenarios were developed after reviewing studies submitted by the registrant and review of the label use patterns.

Since a variety of plastic products contain the Dolphin antimicrobial, residential consumers might be exposed daily to more than one Dolphin-impregnated product. Therefore, both individual and aggregate risks from using Dolphin-containing plastic

products were assessed. In addition, since residential consumers might be exposed to a Dolphin-impregnated plastic product daily for a long period of time, both short term and intermediate risks were assessed. The residential exposures were assessed using the EPA standard exposure scenarios (EPA, 1997a). The occupational exposure was assessed based on the maximum airborne concentration of Dolphin monitored during production of a PVC master batch in a United Kingdom (UK) facility.

3.0 STUDIES CONDUCTED BY THE REGISTRANT

This exposure/risk assessment was based on the following studies/information submitted to EPA by the Registrant, Avecia Inc., Wilmington, DE:

- Residential and Aggregate Risk Assessments for Exposure to Products Containing Vanquish® (MRID# 450830-01).
- On Site Monitoring at Astropol (MRID# 45083-02).
- Review of Dolphin 100 Antimicrobial Inhalation Monitoring Data (MRID# 450830-03).
- Dolphin 100 Antimicrobial Product Use Information (MRID # 450830-05).
- Dolphin 100 Antimicrobial Post-Application Exposure (MRID # 450830-06).

4.0 USES OF DOLPHIN ANTIMICROBIALS

According to EPA registrations No. 72674-G (Vanquish Phthalate) (Avecia Inc., 2000d) and No. 72674-E (Vanquish 100) (Avecia Inc., 2000e), the active ingredient of Dolphin 100 (i.e., Vanquish) antimicrobials is N-Butyl-1,2- Benzisothiazolin-3-one. Currently, both a manufacturing use product (MUP) and an end use product (EUP) are marketed. Registration No. 72674-G product, which is the EUP, contains 9.5 percent of the active ingredient, while the MUP (Registration No. 72674-E) contains 97.8 percent of the active ingredient. The recommended concentrations of the active ingredient in plastic products range from 0.03 percent to 1.0 percent, as shown in Table 1.

Table 1. Application Rates of Dolphin Antimicrobials in Plastic Materials As Recommended by the Label

Application	Percent of Dolphin 100 ¹
Plasticized PVC	0.03 to 0.5
Polyurethane	0.05 to 0.5
Silicones	0.05 to 1.0
Polyesters	0.05 to 1.0
Polyolefins	0.05 to 1.0
Acrylics	0.05 to 1.0
Synthetic elastomers	0.03 to 1.0
Natural Latex rubber	0.03 to 0.5

1. Dolphin 100 or Vanquish 100 contains 97.8 percent of the active ingredient.
2. Table was prepared based on Avecia Inc., 2000e.

Dolphin antimicrobial is used as an industrial preservative to prevent growth of fungi and bacteria in plastic products. The plastic materials frequently treated with Dolphin antimicrobial include (Novigen Inc., 2000):

1. Polyvinyl chloride (PVC);
3. Polyurethane (PU);
4. Silicone; and
5. Acrylics.

The Dolphin-impregnated plastic materials are used to make a variety of products. Some typical end-use of Dolphin-impregnated products are provided in Table 2. Note that the Dolphin-treated plastic materials are restricted for use in the manufacture of any product which might come in contact with food. Thus, presumably, there is no dietary exposure to Dolphin through use of plastic products.

Table 2. Uses of Dolphin - Treated Plastic Materials

<p><u>Polyurethane Products</u> Foam mattress Foam cushioning in foot wear Foam seating Artificial leather with nylon or fabric lining Molded automotive parts (e.g., door seals and shock absorbers)</p> <p><i>Worse-case use scenario for polyurethane-containing products : Foam mattress</i></p>
<p><u>Silicones</u> Bathtub/shower caulks Industrial caulks and sealants Adhesives</p>
<p><u>Polyvinylchloride</u> Shower curtains Synthetic leather (e.g. sneakers and training shoe uppers) Swimming pool, pond, and ditch liners PVC coated wires Vinyl flooring Vinyl wall covering Tarpaulins Awnings Tubing (e.g. garden hose, marine hose and sleeving, etc.)</p> <p><i>Worst-case use scenarios for polyvinylchloride-containing products: Shower Curtains and Toys</i></p>

5.0 SUMMARY OF TOXICITY CONCERNS IMPACTING OCCUPATIONAL AND RESIDENTIAL EXPOSURES

According to the information submitted by the registrant (Novigen Inc., 2000.), a No Adverse Effect Level (NOAEL) of 300 mg/kg bw/day for short term exposure has been identified from an short term rat development toxicity study. In the study, ossification of the *manus* and the 5th sternebra were observed. This NOAEL was used in both the incidental and dermal exposures. Since no dermal exposure study was conducted, it was assumed that 100% of the residues in contact with the skin would be absorbed. A Margin of Exposure (MOE) greater than 100 is considered acceptable for short term exposures to Dolphin antimicrobial.

A No Observed Effect Level (NOEL) of 15 mg/kg bw/day (Novigen, 2000) has been identified for intermediate-term exposures to Dolphin antimicrobial. This NOEL was determined from a 90 day rat feeding study. Since no dermal absorption study was conducted, it was assumed that 100 percent of residues in contact with skin will be absorbed. A MOE greater than 100 is considered acceptable for intermediate exposures.

The NOAEL and NOEL values above were provided in the exposure assessment study submitted by the registrant (Novigen Inc., 2000). However, the source of these toxicity values was not provided in the registrant's study report. No toxicological end points are available from AD at this time for this assessment (Personal Communication with Dr. Tim McMahon, 2001).

6.0 HANDLER AND POST-APPLICATION EXPOSURES/ASSUMPTIONS

EPA has determined that there are potential application/post-application exposures to Dolphin anti-microbials during manufacturing and residential consumer use of Dolphin-impregnated plastic products. In order to determine the magnitude of occupational and residential exposures, the following exposure scenarios were considered in this exposure assessment:

- **Primary Occupational Handlers** - Workers in a manufacturing setting who are mixing Dolphin with plastic materials and obtruding plastic products;
- **Residential Consumer Post-Application Exposure** - Residential consumers who are exposed to Dolphin antimicrobials due to use of the following products: foam mattresses, shower curtains, and toys.

Occupational post-application exposure was not assessed because post-application exposure to Dolphin-impregnated plastic products is expected to be insignificant, compared to exposure to primary occupational handlers. In addition, there is no need to consider residential application exposure since Dolphin antimicrobials are incorporated into plastic products during the manufacturing process. In subsequent sections, the exposure and risk for each of the above exposure scenarios were estimated and described.

7.0 PRIMARY OCCUPATIONAL HANDLERS

During manufacturing of plastic products, occupational workers may be exposed to Dolphin antimicrobials during incorporation of Dolphin into plastic materials and extrusion of plastic products. The registrant (Avecia Inc.) did not conduct an on-site monitoring study, but did obtain and review a copy of the study report entitled "On Site Monitoring at Astropol." This study was conducted by Rapra Technology LTD (Avecia Inc., 1999) to monitor airborne concentrations of Dolphin antimicrobial during production of a polyvinyl chloride masterbatch in a UK facility - Astropol. The study used impregnated polyvinyl chloride contained 4.57 percent of the Dolphin 100 antimicrobial (Dolphin 100 contains 97.7 percent of the active ingredient), which is 4.57 times higher than the maximum label application rate of 1 percent (EPA Registration No. 72674-E). In this assessment, the maximum airborne concentration monitored was used to estimate worker inhalation

exposure. Dermal exposure was not assessed because workers wear protective equipment and are not expected to have dermal contact with plastic products during extrusion.

7.1 Dolphin 100 Antimicrobial Inhalation Monitoring Data

The registrant used inhalation monitoring data submitted by Rapra Technology LTD to support registration of their product. The requirements for inhalation exposure monitoring studies are normally specified by EPA under Series 875.1300 Occupational and Residential Test Guidelines. There is no statement that indicates that this data was initially designed to adhere to these guidelines; therefore, the utility of this data in the exposure assessment is questionable.

The Dolphin 100 Antimicrobial inhalation monitoring data collected by Rapra Technology LTD are provided in Table 3. In this study, two personal air samples were taken. One sample was collected for a worker who mixed Dolphin 100 into raw plastic materials and the other sample was collected for a worker who extruded PVC plastic products. In addition, a total of 10 stationary air samples (including a stack sample) was collected at the mixing platform and at the extrusion area of the production facility. The analytical limit of detection in this study was 0.003 mg/m^3 for a 530 liter air sample.

As shown in Table 3, airborne concentrations of Dolphin in stationary air samples were at levels around the limit of detection. Dolphin concentration in the personal air sample for the mixer is less than the limit of detection, suggesting that the exposure to the mixer is small. However, Dolphin concentration in the personal air sample collected for the worker extruding the PVC was 0.017 mg/m^3 . The highest concentration of 0.419 mg/m^3 was monitored in the stack sample, indicating that the ventilation system was eliminating the Dolphin antimicrobial from the working area.

Since Dolphin 100 was applied at a rate 4.75 times higher than the proposed maximum label rate of 1 percent, it is reasonable to assume that the airborne concentrations monitored in the study represent the worst-case scenario. In the study review report submitted by the Registrant (Avecia Inc., 2000a), the airborne concentrations were further adjusted by extrapolating the Dolphin content from 4.75 percent to 1.0 percent. The adjusted concentrations are also provided in Table 3. Since the Registrant did not provide data which could demonstrate the proportionality between airborne concentrations and Dolphin content in the PVC product, the unadjusted concentrations were used in this exposure assessment. Thus, the maximum unadjusted airborne concentration of 0.017 mg/m^3 for the PVC extruding worker was used to estimate occupational exposure in this assessment.

Table 3. Airborne Concentrations of Dolphin During Production of a Polyvinyl chloride (PVC) Master Batch at Astropol, UK

Sample Types	Workers Monitored/Locati-on Monitored	Sampling Date	Sampling Time (Minutes)	Flow Rate (L/min)	Volume Sampled (L)	Analyte	Mass on Filters (μg)	Airborne Concentr-ations (mg/m^3)	Adjusted Airborne Concentration (mg/m^3)
Personal Air Samples	The worker who mixed and blended raw materials	26-Feb-99	268	2.0	536	Dolphin	< 1.5	<0.003	0.0006
	The worker who extruded PVC products	26-Feb-99	254	2.0	508	Dolphin	8.44	0.017	0.0036
Stationary Air Samples	Upper Mixing Platform – Sampler located at head height to right of the mixer lid	26-Feb-99	351	2.0	702	Dolphin	1.51	0.002	0.0004
	Upper Mixing Platform – Sampler located at head height to left of the mixer lid	26-Feb-99	354	2.0	708	Dolphin	2.22	0.003	0.0006
	Upper Mixing Platform – Sampler located at head height on tables in front of the scales	26-Feb-99	352	2.0	704	Dolphin	1.94	0.003	0.0006
	Lower Mixing Platform – Sampler located near the discharge area	26-Feb-99	354	2.0	708	Dolphin	2.43	0.003	0.0006
	Lower Mixing platform – Sampler above hopper	26-Feb-99	261	1.95	509	Dolphin	3.90	0.008	0.0017
	6.3 cm from the extruder dye at head height	26-Feb-99	265	2.0	530	Dolphin	2.84	0.005	0.001

Sample Types	Workers Monitored/Location Monitored	Sampling Date	Sampling Time (Minutes)	Flow Rate (L/min)	Volume Sampled (L)	Analyte	Mass on Filters (µg)	Airborne Concentrations (mg/m ³)	Adjusted Airborne Concentration (mg/m ³)
	2 cm from the extruder dye at head height	26-Feb-99	265	2.0	530	Dolphin	2.64	0.005	0.001
	30 cm from the extruder dye	26-Feb-99	265	2.0	530	Dolphin	2.30	0.004	0.0008
	Background sample at the rear of the production area	26-Feb-99	345	2.0	690	Dolphin	2.15	0.003	0.0006
	Stack sample	26-Feb-99	60	7.0	420	Dolphin	175.93	0.419	0.0882

7.2 Potential Daily Dose

The potential daily dose to Dolphin 100 for occupational workers during production of Dolphin-treated plastic products was estimated using the following equation:

$$PDD = \frac{C_{air} \times I \times H}{W} = \frac{0.017 \text{ mg/m}^3 \times 1.6 \text{ m}^3/\text{hour} \times 8 \text{ hours/day}}{71.8 \text{ kg}} = 0.003 \text{ mg/kg/day}$$

where:

- PDD = Potential daily dose (mg/kg/day)
- C_{air} = Airborne concentration of Dolphin (mg/m³)
- I = Inhalation rate (m³/hour)
- H = Working hours per day
- W = Typical body weight for an adult (kg).

The exposure factors used in the calculation are from EPA's *Exposure Factors Handbook* (EPA, 1997b). C_{air} is from Table 3. The inhalation rate of 1.6 m³/hr is based on short-term exposures at a moderate rate of activity (EPA, 1997b). The body weight of 71.8 kg represents the body weight of all adults and is recommended in EPA (1997b). The working hours are assumed to be 8 hours.

7.3 Margin of Exposure

The Margin of Exposure (MOE) for the exposure scenarios was estimated using the following equation:

$$MOE = \frac{NOAEL \left(\frac{mg}{kg/day} \right)}{Potential \ Daily \ Dose \left(\frac{mg}{kg/day} \right)}$$

where:

NOAEL = No Observable Adverse Exposure Level (mg/kg/day).

According to the Exposure Assessment Report submitted by the Registrant (Novigen Inc., 2000), the NOAEL for short term exposure is 300 mg/kg/day and the NOEL (No Observed Effect Level) for intermediate-term exposure is 15 mg/kg/day. Based on these two toxicity values and a PDD of 0.003 mg/kg/day, the MOE for the short term occupational exposure was estimated to be 100,000 and MOE for intermediate exposure was found to be 5000. Since MOEs for both short term exposure and intermediate term exposure are much larger than the required minimum MOE of 100, the occupational exposure to Dolphin during production of Dolphin-treated plastic products is considered acceptable. However, it should be noted that this conclusion is based on the condition that the ventilation system at the production facility is working well and the workers are wearing appropriate protective equipments, such as gloves, to avoid dermal exposures.

8.0 RESIDENTIAL CONSUMER POST-APPLICATION EXPOSURES

Residential consumers might be exposed to Dolphin via use of a variety of Dolphin-impregnated plastic products. Some examples of Dolphin-containing plastic products are provided in Table 2. In this exposure assessment, exposures to the following three products were selected as worse-case scenarios:

- Foam Mattresses;
- Shower Curtains; and
- Pet Toys.

Since residential consumers might be exposed daily to Dolphin via use of one or more Dolphin-containing products, the aggregate residential consumer exposure to Dolphin was also estimated in the exposure assessment. In the following sections, individual and aggregate dermal exposures to Dolphin due consumer use of the three products above were estimated and described, respectively.

Residential consumer inhalation exposure was considered insignificant due to the following three reasons: (1) the Dolphin antimicrobial is generally contained within the matrix of plastic products; (2) the Dolphin antimicrobial has a low vapor pressure, and (3) the concentrations of Dolphin are less than or equal to 1 percent. Thus, residential inhalation exposure was not estimated in this exposure assessment.

8.1 Leaching Study

In order to estimate the flux rate (or release rate) of Dolphin antimicrobial from plastic products during dermal contact or accidental ingestion, the Registrant conducted two leaching studies with PVC and PU foam materials. PVC and PU materials were impregnated with Dolphin antimicrobial at the label rates of 1 percent and 0.3 percent, respectively. PVC and PU materials were then extracted in synthetic perspiration, synthetic saliva, and water at different time intervals. The results from the leaching studies were provided in the appendices of the exposure assessment report submitted by the registrant (Novigen Inc., 2000) and are re-summarized in Tables 4 and 5. The estimated maximum and average flux rates of Dolphin will be used to represent the short term and intermediate-term flux rates during consumer use of Dolphin-impregnated plastic products.

Table 4. Summary of Leaching Study of Dolphin-Impregnated Polyurethane Foam Materials in Synthetic Perspiration

Sampling Time (hours)	Replicate	Percent Leached (%)	Dolphin Leached ^a (mg)	Flux Rate ^b (mg/cm ² /8 hours)
0	1	3.3	0.495	
	2	2.8	0.42	
0.27	1	6.1	0.915	
	2	5.4	0.81	
0.47	1	7.6	1.14	
	2	6.7	1.005	
0.97	1	9.0	1.35	
	2	8.0	1.2	
1.5	1	10.0	1.5	
	2	9.0	1.35	
1.97	1	10.8	1.62	
	2	9.6	1.44	
3	1	11.6	1.74	
	2	10.3	1.545	
4	1	11.8	1.77	
	2	10.6	1.59	
21.05	1	12.6	1.89	
	2	11.6	1.74	
8 hours	Maximum replicate in the leaching study (i.e., the one at 21.05 hours)	12.6	1.89	0.00378

a Dolphin leached (mg) = 5 g of PU foam × 1,000 mg/g × 0.3 percent of Dolphin in PU foam × Percent leached.

b Flux rate = 1.89 mg/8 hours ÷ 500 cm². Since leaching was not monitored at 8 hours, it was assumed that the percent leached at 21.05 hours be used to represent the percent leached at 8 hours. In addition, the surface area of 5 g of PU foam is 500 cm².

Table 5. Summary of the Leaching Study of Dolphin-Impregnated Polyvinyl Chloride in Synthetic Perspiration, Synthetic Saliva, and Water

Extracting Medium	Sampling Time (hr)	Dolphin Leached (mg)	Flux Rate ^a (mg/m ² /day)	Short term Flux ^b Rate (mg/m ² /day)	Intermediate-term ^c Flux Rate (mg/m ² /day)
Synthetic Perspiration (run 1)	4.58	0.195	166.8	166.8	64.3
	22.9	0.303	51.8		
	50	0.340	26.6		
	118	0.371	12.3		
Synthetic Perspiration (run 2)	4.58	0.193	165.0		
	22.9	0.302	51.6		
	50	0.348	27.3		
	118	0.374	12.4		
Synthetic Saliva (run 1)	4.58	0.192	164.2	164.2	72.2
	22.9	0.246	42.1		
	50	0.124	9.7		
Synthetic Saliva (run 2)	4.58	0.186	159.0		
	22.9	0.290	49.6		
	50	0.115	9.0		
Water	4.58	0.239	204.2	204.2	78.7
	22.9	0.369	63.2		
	50	0.403	31.6		
	118	0.464	15.4		

- a Flux rate (mg/ m²/day) = Dolphin leached (mg) ÷ surface area of plastic sample (61.3 cm²) ÷ sampling time (hr) × 10,000 (cm²/ m²) × 24 (h/day)
- b Short term flux rate = maximum flux rate.
- c Intermediate-term flux rate = average of all flux rates.

8.2 Foam Mattresses

8.2.1 Assumptions

Post-application exposure may occur through dermal contact when residential consumers sleep daily on mattresses containing Dolphin-impregnated polyurethane foam. It was assumed that a cotton sheet would be placed on top of the mattress and provide the same extent of protection as cotton clothing provides to workers handling pesticides in an occupational environment. According to the PHED Surrogate Guidance document (EPA, 1998), the protection factor for cotton clothing is 50 percent. Thus, a protection factor of 50 percent was assumed for a cotton mattress pad.

The flux rate of 0.00378 mg/cm²/8 hours as estimated in the leaching study (Table 4) was used to represent the flux rate of Dolphin from polyurethane foam mattresses. In reality, polyurethane foam would not be saturated in perspiration. Thus, the flux rate from the leaching study is a conservative estimate of the actual flux rate during dermal contact with mattresses.

It should be noted that the flux rate of Dolphin from polyurethane foam was estimated by the Registrant to be 0.00047 mg/cm²/8 hours. The difference is the result of an error in calculating the flux rate in units of mg/cm²/8 hours (Novigen Inc., 2000). The registrant mistakenly divided the amount of Vanquish (i.e., Dolphin) leached in eight hours by 8 when they calculated the flux rate in unit of mg/cm²/8 hours (see Table 9 in Novigen Inc., 2000 for details). Therefore, the correct flux rate of 0.00378 mg/cm²/8 hours as reported in Table 4. This error led to an eight times difference in the flux rate and subsequently in MOEs between the Agency's and the registrant's estimates.

8.2.2 Potential Daily Doses

Based on the EPA Standard Residential Exposure Scenarios for pesticide impregnated products (EPA, 1997a), the potential daily dose via dermal exposure was estimated using the following equation:

$$PDD = \frac{(FR \div CF) \times 10,000 \text{ cm}^2/\text{m}^2 \times SA \times SL \times PF}{BW}$$

where:

- PDD = Potential Daily Dose (mg/kg/day)
- FR = Flux rate (mg/cm²/8 hours)
- CF = A conversion factor (CF) of 8 is used to convert the flux rate from mg/cm²/8 hours to mg/cm²/hour
- SA = Body surface area (m²)
- SL = Daily average sleeping time (8 hours/day)
- PF = Protection factor from bed sheet (%)
- BW = Body weight (kg)

Table 6. Potential Daily Doses of Dolphin Antimicrobial Due to Dermal Contact with Dolphin-Impregnated Polyurethane Foam Mattresses.

Exposed Population	Flux Rate ^a (mg/cm ² /8 hours)	Contact Body ^b Surface Area (m ²)	Daily Sleeping ^c Time (hours/day)	Protection Factor ^d (%)	Body Weight ^e (kg)	Potential Daily ^f Dose (mg/kg/day)
Adult-Short term Exposure	0.00378	1	8	50	71.8	0.263
Female - Short term Exposure	0.00378	1	8	50	60	0.315
Toddler-Short term Exposure	0.00378	0.35	10	50	15	0.551
Adult-Intermediate Term Exposure	0.00378	1	8	50	71.8	0.263
Female - Intermediate Term	0.00378	1	8	50	60	0.315
Toddler-Intermediate term	0.00378	0.35	10	50	15	0.551

a Based on polyurethane foam leaching study (Avecia, Inc., 2000).

b Based on the Standard Operating Procedures (SOPs) for Residential Exposure Assessments (EPA, 1997).

c Assumed values based on professional judgement.

d Based on the PHED Surrogate Exposure Guide (1998).

e Based on the Standard Operating Procedures (SOPs) for Residential Exposure Assessments (EPA, 1997).

f Potential daily dose = Flux Rate ÷ 8 × 10,000 cm²/m² × Body Surface Area × Sleeping Time × Protection Factor ÷ Body Weight.

The exposure factors used in the calculation and potential daily doses for adults, females and toddlers as estimated are provided in Table 6.

8.2.3 Margin of Exposure (MOE)

The short term and intermediate-term margins of exposure for residential consumers who sleep daily on Dolphin-impregnated polyurethane foam mattresses were estimated, based on the short term NOAEL of 300 mg/kg/day and intermediate-term NOEL of 15 mg/kg/day.

The estimated MOEs are provided in Table 7. The MOEs for short term exposure to adults, females and toddlers are greater than the required MOE of 100. However, MOEs for intermediate term exposures are less than the required MOE of 100.

These results suggest that long-term dermal exposures to Dolphin-impregnated foam mattresses might pose a risk to residential consumers as a result of sleeping daily on these mattresses.

Table 7. Margins of Exposure (MOEs) for Residential Consumers Who Sleep Daily on Dolphin-Impregnated Polyurethane Foam Mattresses

Exposure Scenarios	Margin of Exposures	
	Short term	Intermediate Term
Adult	1140	57
Female	952	48
Toddler	544	27

8.3 Shower Curtains

8.3.1 Assumptions

Residential consumers might be exposed to Dolphin antimicrobial due to dermal contact with Dolphin-impregnated shower curtains during showering. Since no monitoring study was conducted by the registrant, the EPA SOP standard scenarios for pesticide-impregnated products (EPA, 1997a) were used to estimate the exposure. According to EPA standard scenarios, it is assumed that when residential consumers take a shower, 10 percent of their bodies (i.e, 0.2 m² for adults and 0.07 m² for children) would be in contact with a shower curtain for a period of 30 minutes.

The maximum flux rate of 204.2 mg/m²/day and the average flux rate of 78.7 mg/m²/day as determined in the PVC leaching study with water (Table 5) were used to represent the short term flux rate and intermediate-term flux rate, respectively, of Dolphin from shower curtains.

8.3.2 Potential Daily Doses

According to the EPA standard exposure scenarios (EPA, 1997a), potential daily doses of Dolphin antimicrobial for residential consumers due to dermal contact with shower curtains can be estimated using the following equation:

$$PDD = \frac{FR \times SA \times ET}{24 \text{ hours/day} \times BW}$$

where:

PDD = Potential daily dose (mg/kg/day)
 FR = Flux rate of Dolphin from shower curtains (mg/m²/day)
 SA = Surface area of the body which is in contact with shower curtains(m²)
 ET = Exposure time (hours/day)
 BW = Body weight (kg)

The estimated potential daily doses for adults, females, and toddlers are provided in Table 8. The exposure factors used in the calculation are based on the EPA Residential Standard Scenarios (EPA, 1997) and are also provided in Table 8.

8.3.3 Margins of Exposure

The margins of exposure for residential consumers due to dermal contact with shower curtains were estimated based on an short term NOAEL of 300 mg/kg/day and an intermediate-term NOEL of 15 mg/kg/day. The estimated MOEs for adults, females, and toddlers are provided in Table 9. Both short term and intermediate-term MOEs for adults, females, and toddlers are much less than the required minimum MOE of 100. This suggests that little risk is posed to residential consumers using Dolphin-impregnated shower curtains during showering.

8.4 Pet Toys

8.4.1 Assumptions

Dolphin is also used in plastic pet toys to prevent microbial growth and therefore extend the useful life of the toy. Toddlers may be exposed to Dolphin via dermal contact and incidental oral ingestion during playing with Dolphin-impregnated pet toys. An exposure monitoring study was not conducted by the registrant. Therefore, the exposure to toddlers was assessed based on the EPA Residential Standard Scenarios (EPA, 1997a).

Table 8. Potential Daily Doses of Dolphin Antimicrobial Due to Dermal Contact with Dolphin-Impregnated Shower Curtain Curtains

Exposed Population	Flux Rate ^a (mg/ m ² /day)	Contact Body ^b Surface Area (m ²)	Exposure Time ^c (hours/day)	Body Weight ^d (kg)	Potential Daily ^e Dose (mg/kg/day)
Adult-Short term Exposure	204.2	0.2	0.5	71.8	0.01185
Female-Short term Exposure	204.2	0.2	0.5	60	0.01418
Toddler- Short term Exposure	204.2	0.07	0.5	15	0.01985
Adult-Intermediate Term Exposure	78.7	0.2	0.5	71.8	0.00457
Female-Intermediate Term Exposure	78.7	0.2	0.5	60	0.00547
Toddler-Short term Exposure	78.7	0.07	0.5	15	0.00765

a Based on PVC leaching study (Avecia, Inc., 2000).

b Based on the Standard Operating Procedures (SOPs) for Residential Exposure Assessments (EPA, 1997a).

c Based on the Standard Operating Procedures (SOPs) for Residential Exposure Assessments (EPA, 1997a).

d Based on the Standard Operating Procedures (SOPs) for Residential Exposure Assessments (EPA, 1997a).

e Potential daily dose = Flux Rate ÷ 24 hours/day × Body Surface Area × Exposure Time ÷ Body Weight.

Table 9. Margins of Exposure for Residential Consumer Exposure Due to Dermal Contact with Shower Curtains

Exposure Scenarios	Margin of Exposures	
	Short Term	Intermediate Term
Adult	25316	3284
Female	21155	2745
Toddler	15111	1960

8.4.2 Potential Daily Dose from Dermal Contact

The EPA Residential SOPs (EPA, 1997a) do not have a specific scenario for toddler's dermal exposure to pesticide-impregnated pet toys. Thus, the potential daily doses due to dermal contact were estimated using the same equation as for shower curtains and mattresses. However, it was assumed that dermal exposure occurred only through exposure to the hands of a toddler. The surface area of both hands of a toddler is about 5 percent of the total body surface area of 0.7 m², i.e. 0.035 m² (EPA, 1997a).

The maximum and average flux rates of 166.8 mg/m²/day and 64.3 mg/m² of Dolphin-impregnated PVC in synthetic perspiration (Table 5), as estimated in the PVC leaching study by the Registrant, were used to represent the short term and intermediate-term flux rates of Dolphin from pet toys during dermal contact with hands, respectively.

Based on the above assumptions, potential daily doses due to dermal contact with pet toys were estimated using the following equation:

$$PDD = \frac{FR \times SA \times ET}{24 \text{ hours/day} \times BW}$$

where:

- PDD = Potential daily dose (mg/kg/day)
- FR = Flux rate of Dolphin from pet toys (mg/m²/day)
- SA = Surface area of toddler's hands (m²)
- ET = Exposure time (hours/day)
- BW = Body weight (kg)

The estimated short term and intermediate term potential daily dermal doses for toddlers who play with pet toys are provided in Table 10.

Table 10 Potential Daily Doses of Dolphin Due to Dermal Exposure During Playing with Dolphin-Impregnated Pet Toys

Exposure Scenarios	Flux Rate (mg/m ² /day)	Hand Surface Area (m ²)	Exposure Time (hours)	Body Weight (kg)	Potential Daily Dose (mg/kg/day)
Toddler - short term dermal exposure	166.8	0.035	1	15	0.0162
Toddler - intermediate term dermal exposure	64.3	0.035	1	15	0.0063

8.4.3 Potential Daily Doses from Incidental Oral Ingestion

Potential daily doses due to incidental oral ingestion for toddlers playing with Dolphin-impregnated pet toys were estimated based on the EPA Residential Standard Scenarios (EPA, 1997a). The EPA Residential SOPs assume that toddlers would mouth pet toys once per day when they play with pet toys. It was also assumed that the total surface area of a pet toy was 500 cm² and the typical weight of a toddler was 15 kg. The maximum and average flux rates of 164.2 mg/m²/day and 72.2 mg/m²/day (Table 5), as estimated in the PVC leaching study with synthetic saliva, were used to represent the short term and intermediate-term flux rates, respectively, of Dolphin from pet toys during mouthing. The potential daily doses due to incidental oral ingestion were estimated using the following equation:

$$PDD = \frac{FR \times SA \times ET}{24 \text{ hours/day} \times BW}$$

where:

- PDD = Potential Daily Dose (mg/kg/day)
- FR = Flux Rate of Dolphin via saliva from pet toys (mg/m²/day)
- SA = Surface Area of a pet toy (m²)
- ET = Exposure Time (hours/day)
- BW = Body Weight (kg)

The estimated potential daily doses of Dolphin for toddlers due to oral ingestion while playing with pet toys are provided in Table 11.

Table 11. Potential Daily Doses of Dolphin Due to Accidental Oral Ingestion During Playing with Dolphin-Impregnated Pet Toys

Exposure Scenarios	Flux Rate (mg/m ² /day)	Surface Area of Products (m ²)	Exposure Time (hours)	Body Weight (kg)	Potential Daily Dose (mg/kg/day)
Toddler-Short term	164.2	0.05	1	15	0.0228
Toddler - Intermediate Term	72.2	0.05	1	15	0.010

7.4.4 Margins of Exposures

The margins of exposure for toddlers playing with pet toys were estimated, based on the short term NOAEL of 300 mg/kg/day and intermediate-term NOEL of 15 mg/kg/day. The estimated dermal and oral MOEs for short term and intermediate-term exposures are much greater than the required minimum MOE of 100, as shown in Table 12. The MOEs for total short term and intermediate-term exposure (i.e., dermal and oral exposures combined, see section 8.5) are also greater than the required minimum MOE of 100. This result suggests that the MOEs are acceptable and there is no probable risk for toddlers playing with pet toy.

Table 12. Margins of Exposure for Toddlers Playing With Dolphin-Impregnated Pet Toys

Exposure Scenarios	Margin of Exposures	
	Short Term	Intermediate Term
Dermal Exposure	18499	2399
Incidental Oral Ingestion	13154	1500
Total Exposure (i.e., dermal and oral)	7688	921

8.5 Aggregate MOEs

Residential consumers may be exposed to more than one Dolphin-impregnated plastic products daily. Thus, short term and intermediate term aggregate exposure assessments were also conducted. For a worst-case assessment, it was assumed that a residential consumer might be exposed to at least three of the products chosen to represent a worst-case exposure

in one day - shower curtains, mattress foam and pet toys. Aggregate exposures to adults, females, and toddlers were assessed, respectively.

Individual exposures to Dolphin-impregnated products were aggregated based on EPA/OPP Draft Guidance for Performing Aggregate Exposure and Risk Assessments (EPA, 1999). The EPA guidance recommends using the Total MOEs method for aggregating individual exposures. This method requires that individual MOEs have similar uncertainty factors. In the case of Dolphin antimicrobial, the uncertainty factors for all routes of exposure and all sub-population groups are 100. Thus, the following equation was used to aggregate short term and intermediate term exposures.

$$MOE_T = \frac{1}{\frac{1}{MOE_1} + \frac{1}{MOE_2} + \dots + \frac{1}{MOE_n}}$$

where:

- MOE_T = Total or Aggregated Margin of Exposure
- MOE₁ = Margin of Exposure for Dolphin-impregnated product 1
- MOE_n = Margin of Exposure for Dolphin-impregnated product n

The short term and intermediate-term Total Margins of Exposure (i.e, Total MOE) for adults, females, and toddlers as estimated are provided in Table 13. All short term total margins of exposure for assessed populations are greater than the required minimum MOE of 100. This suggests that short term exposure to Dolphin due to use of multiple Dolphin-impregnated products is minimal and there is no probable risk. However, the total MOEs for intermediate-term exposure are less than the required minimum MOE of 100. This results from the intermediate term MOE of < 100 for mattresses. The results indicate that intermediate-term exposure to Dolphin-impregnated plastic products, especially the mattresses, may be of risk to residential consumers.

Table 13. Product-Specific and Aggregate Margins of Exposure (MOEs) for Three-Worst Case Dolphin-Impregnated Plastic Products

Exposed Population	Exposure Route	Exposure Type	Margins of Exposure (MOE)			Aggregate MOEs (Margins of Exposure)
			Pet Toys	Mattresses	Shower Curtain	
Adult	Dermal	Short Term	NA	1140	25316	1091
		Intermediate Term	NA	57	3284	56
Female	Dermal	Short Term	NA	952	21155	911
		Intermediate Term	NA	48	2745	47
Toddler	Dermal	Short Term	18499	544	15111	511
		Intermediate Term	2399	27	1960	26
	Oral Ingestion	Short Term	13155	NA	NA	13155
		Intermediate Term	1500	NA	NA	1500
	Total Exposure (i.e., Dermal and Oral)	Short Term	7688	544	15111	492
		Intermediate Term	881	27	1960	26

9.0 DATA GAPS AND UNCERTAINTIES

The following data gaps and uncertainties critical to the scientific validity and regulatory acceptability are identified and should be considered in using the results of this assessment:

- The registrant used inhalation monitoring data submitted by Rapra Technology LTD to support registration of their product. The requirements for inhalation exposure monitoring studies are normally specified by EPA under Series 875.1300 Occupational and Residential Test Guidelines. There is no statement that indicates that this data was initially designed to adhere to these guidelines; therefore, the utility of this data in the exposure assessment is questionable.
- In the Occupational Inhalation Monitoring Study submitted by the Registrant (Avecia Inc., 1999), only two personal air sample were taken to monitor air exposure concentrations for occupational workers who were extruding PVC plastic products in

the manufacturing setting. However, according to the EPA Pesticide Assessment Guidelines OPPT Series 875, 15 replicates of personal air samples are required to determine exposure concentrations for each exposure scenario.

- Only summaries of the PVC and polyurethane leaching studies are submitted by the Registrant (Novigen Inc., 2000). The summaries are provided as appendices in the Residential Exposure Assessment Study submitted by the Registrant (Novigen Inc., 2000). It is unknown whether the leaching studies were conducted according to the EPA approved protocols or whether appropriate QA/QC samples were used in the leaching studies.
- Toxicological endpoints (i.e., NOAEL and NOEL) used in this assessment are provided in the Registrant-submitted exposure assessment report (Novigen Inc., 2000) "the Residential and Aggregate Risk Assessments for Exposure to Products Containing Vanquish." However, the sources of these toxicity values are not specified. It is unknown whether these toxicity values have been reviewed and accepted by the EPA.
- According to the Residential Exposure Assessment report submitted by the Registrant (Novigen Inc., 2000), intermediate-term MOEs for Dolphin-impregnated polyurethane foam mattresses are greater than 100. However, according to this assessment, intermediate term MOEs for mattresses are less than 100. The difference is the result of an error in calculating the flux rate of Dolphin from polyurethane foam in Table 9 of the Residential Exposure Assessment report submitted by the Registrant (Novigen Inc., 2000). The registrant mistakenly divided the amount of Vanquish (i.e., Dolphin) leached in eight hours by 8 when they calculated the flux rate in unit of $\text{mg}/\text{cm}^2 / 8 \text{ hours}$. Thus, MOEs estimated by the Registrant are 8 times higher than MOEs estimated in this assessment.

10.0 REFERENCES

Avecia Inc. 1999. On Site Monitoring at Astropol. EPA MRID# 450830-02.

Avecia Inc. 2000a. Review of Dolphin 100 Antimicrobial Inhalation Monitoring Data. EPA MRID# 450830-03.

Avecia Inc. 2000b. Dolphin 100 Antimicrobial Product Use Information. EPA MRID# 450830-05.

Avecia Inc. 2000c. Dolphin 100 Antimicrobial Post-Application Exposure. EPA MRID# 45830-06

Avecia Inc. 2000d. Vanquish Phthalate Antimicrobial – An Antimicrobial in Plasticizer for use in the Preservation of Plastics. Draft Label for EPA Registration No. 72674-G.

Avecia Inc. 2000e. Vanquish 100 Antimicrobial for Direct Incorporation into Plastic for Further Processing. Draft Label for EPA Registration No. 72674-E.

EPA. 1997a. Standard Operating Procedures (SOPs) for Residential Exposure Assessments. Prepared by The EPA Residential Exposure Assessment Work Group in December 1997.

EPA. 1997b. Exposure Factors Handbook. EPA/600/P-95/002F. August 1997.

EPA. 1998. PHED Surrogate Exposure Guide.

EPA. 1999. Guidance for Performing Aggregate Exposure and Risk Assessments DRAFT.
Office of Pesticide Programs. February 1, 2000.

Novigen, Inc. 2000. Residential and Aggregate Risk Assessments for Exposure to Products Containing Vanquish®. Sponsored by Avecia, Inc. MRID# 450830-01.

Personal Communication. 2001. Personal communication between Mike Huang, Senior Environmental Scientist and Dr. Timothy McMahon, Toxicologist. February 2001.

File C:\myfiles\2002 reports\ Exposure and Risk Assessment for Dolphin Fungicide (D270047).wpd

CC: Siroos Mostaghimi/RASSB
Chemical Files